REMARKS

Claims 1-41 are currently pending. Claims 1, 2, 4, 6, 7, 19-23 and 26 are currently under examination and are currently rejected. Claims 3, 5, 8-18, 24, 25 and 27-41 are currently withdrawn from consideration. Claim 1 is currently amended.

Applicants thank the Examiner for issuing the Advisory Action mailed October 27, 2005, entering the claim amendments filed in the Amendment of May 23, 2005, withdrawing the outstanding claim rejections under 35 U.S.C. §112, and vacating the non-final Office action of August 10, 2005.

Claim 1 has been amended. Support for the amendment to Claim 1 is found throughout the specification, and in particular at Examples 10 and 11, and as illustrated in Figures 53-61. The amendment to Claim 1 does not introduce new matter.

Claim Rejections Under 35 U.S.C. §102

Claims 1, 2, 4, 6, 7, 19, 20, 21, 22, and 26 remain rejected under 35 U.S.C. §102(b) as allegedly anticipated by Müller *et al.* (1998, *FEBS Lett* 422:259-264). Applicants respectfully traverse this rejection for the reasons presented below.

To anticipate a claim, the reference must teach every element of the claim. "'A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.'" MPEP § 2131, quoting *Verdegaal Bros. v. Union Oil Co. of California,* 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Here, Claim 1 recites a multifunctional compound expressed in and secreted by a mammalian host cell as a fully functional heterodimer of two polypeptide chains, wherein one of the polypeptide chains includes the constant CH1-domain of an immunoglobulin heavy chain and the other polypeptide chain includes the constant CL-domain of an immunoglobulin light chain, and the polypeptide chains of the multifunctional compound further include four polypeptide functional domains fused to the constant domains, where the functional domains have different receptor or ligand functions, and at least two of the different functional domains lack an intrinsic affinity for one another, and wherein the polypeptide chains are linked via the constant domains.

In contrast, Müller *et al.* discloses the functional expression of bispecific antibodies in *E. coli* using plasmid constructs designed for recombinant expression of proteins in *E. coli* (*e.g.*, Materials and Methods, page 259 right column, to page 261, left column). Therefore, the rejection of independent Claim 1 and dependent claims 2, 4, 6, 7, 19, 20, 21, 22, and 26 under 35 U.S.C. §102(b) is improper and should be withdrawn.

Claim Rejections Under 35 U.S.C. §103

Claims 1, 2, 4, 6, 7, 19, 20, 21, 22, 23, and 26 remain rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Müller *et al.*, in view of Plückthun and Pack (1997, *Immunotechnology* 3:83-105). Müller *et al.* allegedly discloses a multifunctional compound with all the structural limitations of the rejected claims, for reasons given for the rejection under 35 USC §102(b), but it is admitted that Müller *et al.* does not specifically teach the upper hinge region of human IgG3. Plückthun and Pack allegedly teach the use of hinge regions, in particular the upper hinge from human IgG3. Based on these disclosures, it would allegedly have been obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute the linkers of Müller *et al.*, with the upper hinge region of human IgG3 taught by Plückthun and Pack, to make a multifunctional compound. Applicants respectfully traverse for the reasons presented below.

Criteria for establishing a prima facie case of obviousness

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference, or references when combined, must teach or suggest all the claim limitations. *See*, MPEP §§ 2142, 2143.

The combination of references does not teach or suggest all claim limitations

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka,* 490 F.2d 981, 180 USPQ 580 (CCPA 1974). For the reasons set forth in traversing the 35 U.S.C. §102(b) rejection above, Müller *et al.* does not teach or suggest the claim limitations set forth in amended Claim 1. In addition, applicants do not find any teaching or suggestion in Plückthun and Pack of the claim limitations set forth in Claim 1. Moreover, applicants do not find any teaching or suggestion in Plückthun and Pack that the *E. coli*-produced bispecific antibodies of Müller *et al.* can be expressed in and secreted by a mammalian host cell. Therefore, the cited combination of references do not teach or suggest all the limitations of the claimed invention and a *prima facie* case of obviousness has not been established.

The combined references do not provide a suggestion or motivation to make the claimed invention

According to the MPEP, the prior art must suggest the desirability of the claimed invention. MPEP §2143.01 Obviousness can only be established by combining or modifying

the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *In re Fine*, 837 F.2d 1071, 5 USPQ 2d 1596 (Fed. Cir. 1988); *In re Jones* 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). *See generally*, MPEP §2143. Here, there is no teaching, suggestion, or motivation in the Müller *et al.* reference or the Plückthun and Pack reference to combine the teachings of these references to produce the claimed invention.

The primary reference, Müller *et al.*, discloses the functional expression of bispecific antibodies in *E. coli* using plasmid constructs designed for recombinant expression of bispecific antibodies in *E. coli*, and does not teach or suggest the claimed invention. Applicants do not find a teaching or suggestion in the secondary reference, Plückthun and Pack, to modify the *E. coli*-expressed bispecific antibodies of Müller *et al.* to produce the claimed multifunctional compound.

Because the cited combination of references does not teach the claimed invention, and because there is no teaching, suggestion, or motivation in the cited references to combine the teachings of these references to produce the claimed invention, the criteria for a *prima facie* case of obviousness have not been satisfied and no *prima facie* case of obviousness has been established. Therefore, the rejection of Claims 1, 2, 4, 6, 7, 19, 20, 21, 22, 23, and 26 under 35 U.S.C. §103 is improper and should be withdrawn.

CONCLUSION

Claims 1-41 are currently pending. Claims 1, 2, 4, 6, 7, 19-23 and 26 are currently under examination. Claims 3, 5, 8-18, 24, 25 and 27-41 are currently withdrawn from consideration. Claim 1 is currently amended. Applicants maintain that the amended claims clearly and patentably define the invention, and respectfully request allowance of the claims now pending.

Please charge any fees associated with the submission of this paper to Deposit Account Number 03-3975. The Commissioner for Patents is also authorized to credit any over payments to the above-referenced Deposit Account.

Respectfully submitted,
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